

What is claimed is

1. ~~A process for separating outer birch bark from inner birch bark~~  
comprising subjecting birch bark to at least one of fragmentation and  
5 pelletization to provide a combination of outer birch bark shreds and inner birch  
bark chunks or outer birch bark pellets and inner birch bark chunks; and  
separating the outer birch bark shreds or outer birch bark pellets from the inner  
birch bark chunks.
- 10 2. The process of claim 1 wherein the separating comprises pushing  
the outer birch bark shreds through a mesh effective to separate the outer birch  
bark shreds from the inner birch bark chunks or the separating is accomplished  
with the use of an air classifier.
- 15 3. The process of claim 1 or 2 wherein the fragmentation is  
accomplished with a chipper or a shredder and the pelletization is accomplished  
with a pellet machine.
4. ~~The process of claim 1 or 2 further comprising reducing the size~~  
20 ~~of the outer birch bark shreds with the use of a hammermill.~~
5. A process for obtaining a natural product from outer birch bark  
comprising subjecting the outer birch bark to supercritical fluid extraction to  
provide the natural product.
- 25 6. The process of claim 5 wherein the natural product is betulin,  
betulinic acid or lupeol.
7. The process of claim 5 wherein the supercritical fluid extraction  
30 utilizes carbon dioxide as a solvent.

8. The process of claim 5, wherein the supercritical fluid extraction utilizes carbon dioxide; at least one of Xe, Freon-23, ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane, ammonia, and n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O; at least one of THF, methylene chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, and *p*-Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>; and optionally at least one of  
5 methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol, 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene, hexanes, and pentanes; as a solvent.

10

9. A process for obtaining lupeol, betulinic acid and betulin from outer birch bark comprising:

extracting with carbon dioxide at a pressure between about 3,000 psi and 10,000 psi and at a temperature between about 50°C and 100°C to  
15 provide lupeol, betulin and betulinic acid.

10. A process for obtaining lupeol, betulinic acid and betulin from outer birch bark using fractional supercritical fluid extraction comprising:

extracting with carbon dioxide at a pressure below about 5,000  
20 psi and at a temperature below about 50°C to provide a product comprising lupeol; and

extracting with carbon dioxide at a pressure of about 5,000 psi to about 10,000 psi and at a temperature of about 50°C to about 120°C to provide a product comprising a mixture of betulin and betulinic acid.

25

11. The process of claim 10 further comprising separating the betulin from the mixture of betulin and betulinic acid.

12. A process for obtaining lupeol from outer birch bark comprising:

30 subjecting the outer birch bark to supercritical fluid extraction with carbon dioxide at a temperature of about 40°C to about 50°C and a pressure

of about 3,000 psi to about 5,000 psi for a period of time of about 1 hour to about 3 hours to provide the lupeol.

13. A process for obtaining lupeol, betulinic acid and betulin from  
5 outer birch bark comprising:

extracting with carbon dioxide; at least one of Xe, Freon-23,  
ethane,  $N_2O$ ,  $SF_6$ , propane, ammonia, and  $n-C_4H_{10}$ ,  $(C_2H_5)_2O$ ; at least one of  
THF, methylene chloride, chloroform,  $C_6H_5CF_3$ , and  $p-Cl-C_6H_4-CF_3$ ; and  
optionally at least one of methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol,  
10 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane,  
ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl  
sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene,  
hexanes, and pentanes; at a pressure between about 3,000 psi and 10,000 psi and  
at a temperature between about 50°C and 100°C to provide lupeol, betulin and  
15 betulinic acid.

14. A process for obtaining lupeol, betulinic acid and betulin from  
outer birch bark using fractional supercritical fluid extraction comprising:  
extracting with carbon dioxide; at least one of Xe, Freon-23,  
20 ethane,  $N_2O$ ,  $SF_6$ , propane, ammonia, and  $n-C_4H_{10}$ ,  $(C_2H_5)_2O$ ; at least one of  
THF, methylene chloride, chloroform,  $C_6H_5CF_3$ , and  $p-Cl-C_6H_4-CF_3$ ; and  
optionally at least one of methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol,  
2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane,  
ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl  
25 sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene,  
hexanes, and pentanes; at a pressure below about 5,000 psi and at a temperature  
below about 50°C to provide a product comprising lupeol; and

extracting with carbon dioxide; at least one of Xe, Freon-23,  
ethane,  $N_2O$ ,  $SF_6$ , propane, ammonia, and  $n-C_4H_{10}$ ,  $(C_2H_5)_2O$ ; at least one of  
30 THF, methylene chloride, chloroform,  $C_6H_5CF_3$ , and  $p-Cl-C_6H_4-CF_3$ ; and  
optionally at least one of methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol,  
2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane,

ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene, hexanes, and pentanes; at a pressure of about 5,000 psi to about 10,000 psi and at a temperature of about 50°C to about 120°C to provide a product comprising a mixture of betulin and betulinic acid.

15. The process of claim 14 further comprising separating the betulin from the mixture of betulin and betulinic acid.

10 16. A process for obtaining lupeol from outer birch bark comprising: subjecting the outer birch bark to supercritical fluid extraction with carbon dioxide; at least one of Xe, Freon-23, ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane, ammonia, and n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O; at least one of THF, methylene chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, and *p*-Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>; and optionally at least one of  
15 methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol, 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene, hexanes, and pentanes; at a temperature of about 40°C to about 50°C and a pressure of about  
20 3,000 psi to about 5,000 psi for a period of time of about 1 hour to about 3 hours to provide the lupeol.

17. A process for isolating 9,10-epoxy-18-hydroxyoctadecanoic acid from outer birch bark comprising:  
25 (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second outer birch bark and a second solution;  
(2) separating the second solution from the second outer birch bark;  
30 (3) condensing the second solution at a temperature below about 50°C to form a third solution;



(9) subjecting the sixth solution to epoxidizing conditions to provide an epoxide and hydrolyzing the epoxide to provide a seventh solution; and

(10) crystallizing the seventh solution to give 9,10,18-  
5 trihydroxyoctadecanoic acid.

21. The process of claim 20 wherein lupeol, betulinic acid and betulin are removed from the outer birch bark prior to the alkali hydrolysis.

10 22. The process of claim 20 further comprising recrystallizing the 9,10,18-trihydroxyoctadecanoic acid from an alcohol or an aqueous alcohol solution.

23. A process for isolating non-soluble polyphenolic polymers and  
15 fatty acids from outer birch bark comprising:

- (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second birch bark and a second solution;
- (2) separating the second solution from the second outer birch bark;
- 20 (3) adding water to the second outer birch bark to provide a third solution and a third outer birch bark;
- (4) separating the third solution from the third outer birch bark;
- (5) acidifying the third solution to a pH of about 3.0 to about 4.0 to give a fourth solution and a mixture of non-soluble polyphenolic polymer and  
25 fatty acids; and
- (6) separating the mixture of fatty acids and non-soluble polyphenolic polymers from the fourth solution.

24. The process of claim 23 wherein lupeol, betulinic acid and betulin  
30 are removed from the outer birch bark prior to the alkali hydrolysis.

25. A process for isolating fatty acids and soluble polyphenolic polymers from outer birch bark comprising:

- (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second outer birch bark and a second solution;
- (2) separating the second solution from the second outer birch bark;
- (3) adding water to the second outer birch bark to provide a third outer birch bark and a third solution;
- (4) separating the third solution from the third outer birch bark;
- (5) acidifying the third solution to a pH of about 3.0-4.0 to give a fourth solution and a solid;
- (6) separating the solid from the fourth solution;
- (7) adding an alcohol to the fourth solution to provide a fifth solution and a precipitate;
- (8) separating the precipitate from the fifth solution; and
- (9) condensing the fifth solution to provide a mixture of fatty acids and soluble polyphenolic polymers.

26. The process of claim 25 wherein lupeol, betulinic acid and betulin are removed from the outer birch bark prior to the alkali hydrolysis.

27. A process for separating outer birch bark from inner birch bark comprising subjecting birch bark to at least one of fragmentation and pelletization to provide a combination of outer birch bark shreds and inner birch bark chunks or outer birch bark pellets and inner birch bark chunks; and separating the outer birch bark shreds or outer birch bark pellets from the inner birch bark chunks.

28. The process of claim 27 wherein the separating comprises pushing the outer birch bark shreds through a mesh effective to separate the

outer birch bark shreds from the inner birch bark chunks or the separating is accomplished with the use of an air classifier.

29. The process of claim 27 or 28 wherein the fragmentation is accomplished with a chipper or a shredder and the pelletization is accomplished with a pellet machine.

30. The process of claim 27 or 28 further comprising reducing the size of the outer birch bark shreds with the use of a hammermill.

31. A process for obtaining a natural product from outer birch bark comprising subjecting the outer birch bark to supercritical fluid extraction to provide the natural product.

32. The process of claim 31 wherein the natural product is betulin, betulinic acid or lupeol.

33. The process of claim 31 wherein the supercritical fluid extraction utilizes carbon dioxide as a solvent.

34. The process of claim 31 wherein the supercritical fluid extraction utilizes carbon dioxide and at least one of Xe, Freon-23, ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane, ammonia, n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O, THF, methylene chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, *p*-Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>, methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol, 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene, hexanes, and pentanes; as a solvent.

35. A process for obtaining lupeol, betulinic acid and betulin from outer birch bark comprising:



extracting with carbon dioxide at a pressure between about 3,000 psi and 10,000 psi and at a temperature between about 50°C and 100°C to provide lupeol, betulin and betulinic acid.

- 5 36. A process for obtaining lupeol, betulinic acid and betulin from outer birch bark using fractional supercritical fluid extraction comprising:

extracting with carbon dioxide at a pressure below about 5,000 psi and at a temperature below about 50°C to provide a product comprising lupeol; and

- 10 extracting with carbon dioxide at a pressure of about 5,000 psi to about 10,000 psi and at a temperature of about 50°C to about 120°C to provide a product comprising a mixture of betulin and betulinic acid.

- 15 37. The process of claim 36 further comprising separating the betulin from the mixture of betulin and betulinic acid.

38. A process for obtaining lupeol from outer birch bark comprising: subjecting the outer birch bark to supercritical fluid extraction with carbon dioxide at a temperature of about 40°C to about 50°C and a pressure of about 3,000 psi to about 5,000 psi for a period of time of about 1 hour to about 3 hours to provide the lupeol.

39. A process for obtaining lupeol, betulinic acid and betulin from outer birch bark comprising:
- 25 extracting with carbon dioxide and at least one of Xe, Freon-23, ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane, ammonia, n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O, THF, methylene chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, p-Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>, methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol, 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-
- 30 dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene, hexanes, and pentanes; at a pressure between about

3,000 psi and 10,000 psi and at a temperature between about 50°C and 100°C to provide lupeol, betulin and betulinic acid.

40. A process for obtaining lupeol, betulinic acid and betulin from  
5 outer birch bark using fractional supercritical fluid extraction comprising:  
extracting with carbon dioxide and at least one of Xe, Freon-23,  
ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane, ammonia, n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O, THF, methylene  
chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, *p*-Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>, methanol, ethanol, 1-propanol,  
2-propanol, 1-hexanol, 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane,  
10 acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-  
dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide,  
acetone, propane, toluene, hexanes, and pentanes; at a pressure below about  
5,000 psi and at a temperature below about 50°C to provide a product  
comprising lupeol; and  
15 extracting with carbon dioxide and at least one of Xe, Freon-23,  
ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane, ammonia, n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O, THF, methylene  
chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, *p*-Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>, methanol, ethanol, 1-propanol,  
2-propanol, 1-hexanol, 2-methoxy ethanol, tetrahydrofuran, 1,4-dioxane,  
acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-  
20 dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide,  
acetone, propane, toluene, hexanes, and pentanes; at a pressure of about 5,000  
psi to about 10,000 psi and at a temperature of about 50°C to about 120°C to  
provide a product comprising a mixture of betulin and betulinic acid.

- 25 41. The process of claim 40 further comprising separating the betulin  
from the mixture of betulin and betulinic acid.

42. A process for obtaining lupeol from outer birch bark comprising:  
subjecting the outer birch bark to supercritical fluid extraction  
30 with carbon dioxide and at least one of Xe, Freon-23, ethane, N<sub>2</sub>O, SF<sub>6</sub>, propane,  
ammonia, n-C<sub>4</sub>H<sub>10</sub>, (C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>O, THF, methylene chloride, chloroform, C<sub>6</sub>H<sub>5</sub>CF<sub>3</sub>, *p*-  
Cl-C<sub>6</sub>H<sub>4</sub>-CF<sub>3</sub>, methanol, ethanol, 1-propanol, 2-propanol, 1-hexanol, 2-methoxy

ethanol, tetrahydrofuran, 1,4-dioxane, acetonitrile, dichloromethane, ammonia, chloroform, propylene carbonate, N,N-dimethylacetamide, dimethyl sulfoxide, formic acid, water, carbon disulfide, acetone, propane, toluene, hexanes, and pentanes; at a temperature of about 40°C to about 50°C and a pressure of about 3,000 psi to about 5,000 psi for a period of time of about 1 hour to about 3 hours to provide the lupeol.

43. A process for isolating 9,10-epoxy-18-hydroxyoctadecanoic acid from outer birch bark comprising:

- (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second outer birch bark and a second solution;
- (2) separating the second solution from the second outer birch bark;
- (3) condensing the second solution at a temperature below about 50°C to form a third solution;
- (4) adding water to the third solution to form a precipitate and a fourth solution;
- (5) separating the precipitate from the fourth solution;
- (6) acidifying the fourth solution to a pH of about 5.5 to about 6.5 to give a fifth solution and 9,10-epoxy-18-hydroxydecanoic acid as a precipitate; and
- (7) separating the 9,10-epoxy-18-hydroxydecanoic acid precipitate from the fifth solution to give 9,10-epoxy-18-hydroxydecanoic acid.

44. The process of claim 43 wherein lupeol, betulin and betulinic acid are removed from the outer birch bark prior to the alkali hydrolysis.

45. The process of claim 43 further comprising recrystallizing the 9,10-epoxy-18-hydroxydecanoic acid from isopropanol, methanol or ethanol.

46. A process for isolating 9,10,18-trihydroxyoctadecanoic acid from outer birch bark comprising:

- (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second outer birch bark and a second solution;
- (2) separating the second solution from the second outer birch bark;
- (3) condensing the second solution at a temperature below about 50°C to form a third solution;
- (4) adding water to the third solution to form a first precipitate and a fourth solution;
- (5) separating the first precipitate from the fourth solution;
- (6) acidifying the fourth solution to a pH of about 5.5 to about 6.5 to give a fifth solution and a second precipitate;
- (7) separating the second precipitate from the fifth solution;
- (8) condensing the fifth solution to provide a sixth solution;
- (9) subjecting the sixth solution to epoxidizing conditions to provide an epoxide and hydrolyzing the epoxide to provide a seventh solution; and
- (10) crystallizing the seventh solution to give 9,10,18-trihydroxyoctadecanoic acid.

47. The process of claim 46 wherein lupeol, betulinic acid and betulin are removed from the outer birch bark prior to the alkali hydrolysis.

48. The process of claim 46 further comprising recrystallizing the 9,10,18-trihydroxyoctadecanoic acid from an alcohol or an aqueous alcohol solution.

49. A process for isolating non-soluble polyphenolic polymers and fatty acids from outer birch bark comprising:

- 10068272-020602
- (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second birch bark and a second solution;
  - (2) separating the second solution from the second outer birch bark;
  - 5 (3) adding water to the second outer birch bark to provide a third solution and a third outer birch bark;
  - (4) separating the third solution from the third outer birch bark;
  - (5) acidifying the third solution to a pH of about 3.0 to about 4.0 to give a fourth solution and a mixture of non-soluble polyphenolic polymer and
  - 10 fatty acids; and
  - (6) separating the mixture of fatty acids and non-soluble polyphenolic polymers from the fourth solution.

50. The process of claim 49 wherein lupeol, betulinic acid and betulin  
15 are removed from the outer birch bark prior to the alkali hydrolysis.

51. A process for isolating fatty acids and soluble polyphenolic polymers from outer birch bark comprising:
- (1) subjecting the outer birch bark to alkali hydrolysis in an aqueous alcohol solution to provide a second outer birch bark and a second  
20 solution;
  - (2) separating the second solution from the second outer birch bark;
  - (3) adding water to the second outer birch bark to provide a third  
25 outer birch bark and a third solution;
  - (4) separating the third solution from the third outer birch bark;
  - (5) acidifying the third solution to a pH of about 3.0-4.0 to give a fourth solution and a solid;
  - (6) separating the solid from the fourth solution;
  - 30 (7) adding an alcohol to the fourth solution to provide a fifth solution and a precipitate;
  - (8) separating the precipitate from the fifth solution; and

(9) condensing the fifth solution to provide a mixture of fatty acids and soluble polyphenolic polymers.

52.           The process of claim 51 wherein lupeol, betulinic acid and betulin  
5   are removed from the outer birch bark prior to the alkali hydrolysis.

10068572, 020602